The Nation’s Best-Kept Secret: Strategies for Promoting Emergency Contraception

Adapted by Jill Gallin, CPNP
Assistant Professor of Clinical Nursing

What if?
A condom broke or slipped off, you had sex when you didn’t expect to, you didn’t use any birth control that weekend, you missed several pills, your diaphragm or cap slipped out of place, you were forced to have sex . . .

Emergency Contraceptives

- Regular contraceptives used in a different way
- Prevent pregnancy after intercourse
- Inhibit ovulation, fertilization, or implantation
- Do not cause abortion

Emergency Contraceptives (cont)

- Will not interrupt or harm an established pregnancy
- Are not the same as mifepristone
- Do not protect against sexually transmitted infections (STIs)

Definition of Pregnancy

- NIH/FDA
  - “Pregnancy encompasses the period of time from confirmation of implantation until expulsion or extraction of the fetus.”
- ACOG
  - “Pregnancy is the state of a female after conception and until termination of the gestation.”
  - “Conception is the implantation of the blastocyst. It is not synonymous with fertilization; synonym: implantation.”

Emergency Contraception: History

- 1500 B.C.
  - Sneezing, hopping, jumping, and dancing
- Douching with various herbs and roots
- Late 1960s
  - Postcoital douching with Coca-Cola™

US Government 1983
Hughes ACOG 1972

Emergency Contraception: History

• 1960s-70s: Diethylstilbesterol (DES) – No longer used because of teratogenicity
• 1974: Yuzpe [pilot study] – 100 µg ethinyl estradiol (EE) with 1.0 mg dl-norgestrel; as effective as DES
• 1977: Yuzpe modified (original dose given twice, 12 hours apart)
• 1984: Yuzpe available in Europe


Women Obtaining Abortions Who Reported Contraceptive Use, by Year

• Intercourse within past 72 hours without contraceptive protection (independent of time in the menstrual cycle)
• Contraceptive mishap – Barrier method dislodgment/breakage – Expulsion of IUD – Missed oral contraceptive pills
• Sexual assault
• Exposure to teratogens (eg, cytotoxic drug)


Emergency Contraception: Indications

Emergency Options in the United States

• Oral contraceptive pills containing estrogen and progestin
• Oral contraceptive pills containing only progestin
• Emergency Copper-T IUD insertion

Conflicting Contraindications: Combined ECPs

• World Health Organization – Confirmed pregnancy
• Faculty of FP and RH Care (United Kingdom) – Confirmed pregnancy – Migraine at presentation (if Hx of focal migraine) – Past Hx of thromboembolism (relative contraindication)
• Planned Parenthood Federation of America – Suspicion or evidence of established pregnancy


Emergency Contraception: History

• 1997: US FDA declares certain OCPs safe and effective for EC
• 1998: FDA approves PREVEN™ (Yuzpe)
• 1998: Large WHO trial reports favorable safety/efficacy data for levonorgestrel EC
• 1999: FDA approves Plan B™ (levonorgestrel)
• 2004: FDA rejects scientific panel recommendation to change Plan B status over-the-counter


PPFA: Manual of Medical Standards and Guidelines 1996
Conflicting Contraindications: Combined ECPs

- **Preven®**
  - Known or suspected pregnancy
  - Pulmonary embolism (current or history)
  - Ischemic heart disease (current or history)
  - History of cerebrovascular accidents
  - Valvular heart disease with complications
  - Severe hypertension
  - Diabetes with vascular involvement
  - Headaches with focal neurological symptoms

Contraindications: Progestin-only ECPs

- **Plan B®**
  - Known or suspected pregnancy
  - Hypersensitivity to any component of the product
  - Undiagnosed abnormal genital bleeding

Emergency Contraceptive Pills: Combined

- Ordinary birth control pills
- Contain estrogen and progestin
- 2 doses of 2 Preven tablets or, for other OCs 2, 4, or 5 pills, depending on brand
- First dose within 72 hours after intercourse
- Second dose 12 hours later
- Side effects: nausea (50%) and vomiting (20%)

Emergency Contraceptive Pills: Progestin-only

- Birth control pills containing only progestin
- 2 doses of 1 Plan B tablet or 20 Ovrette tablets
- First dose within 72 hours after intercourse
- Second dose 12 hours later
- More effective than combined ECPs
- Less nausea and vomiting than with combined ECPs

Copper IUD Insertion

- Copper-T IUD (ParaGard)
- Insertion within 5 days after ovulation (but most protocols state within 5 days after unprotected intercourse)
- 10 more years of highly effective contraception
- Much more effective than ECPs
- Not recommended for women at risk of sexually transmitted infections (STIs)
**Effectiveness**

<table>
<thead>
<tr>
<th>Method</th>
<th># of Pregnancies</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Combined ECPs</td>
<td>20</td>
<td>75%</td>
</tr>
<tr>
<td>Progestin Only ECPs</td>
<td>10</td>
<td>88%</td>
</tr>
<tr>
<td>IUD Insertion</td>
<td>1</td>
<td>99%</td>
</tr>
</tbody>
</table>

*If 1,000 women have unprotected sex once in the second or third week of their cycle*  

---

**How Long After the Morning After?**

**Meta-Analysis of 9 Yuzpe Trials**

| Days  | Pregnancy Rate | p-
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0%</td>
<td>.25</td>
</tr>
<tr>
<td>2</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1.0%</td>
<td></td>
</tr>
</tbody>
</table>

*Trussell et al. Obstet Gynecol 1996;88:150*

---

**How Long After the Morning After?**

**WHO Pooled Data (Yuzpe and LNG)**

| Days  | Pregnancy Rate | p-
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>0.0%</td>
<td>.01</td>
</tr>
<tr>
<td>4-5</td>
<td>0.5%</td>
<td></td>
</tr>
</tbody>
</table>

*Piaggio et al. Lancet 1999;353:721*

---

**How Long After the Morning After?**

**Quebec (Yuzpe)**

| Days  | Pregnancy Rate | p-
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>0.0%</td>
<td>.75</td>
</tr>
<tr>
<td>4-5</td>
<td>1.0%</td>
<td></td>
</tr>
</tbody>
</table>


---

**How Long After the Morning After?**

**Population Council (Yuzpe)**

| Days  | Pregnancy Rate | P-
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0%</td>
<td>0.72</td>
</tr>
<tr>
<td>2</td>
<td>0.5%</td>
<td>0.88</td>
</tr>
<tr>
<td>3</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>4-5</td>
<td>1.5%</td>
<td></td>
</tr>
</tbody>
</table>

*Ellertson et al. Obstet Gynecol 2003, in press*

---

**How Long After the Morning After?**

**Latest WHO Trial (LNG)**

| Days  | Pregnancy Rate | p-
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>0.0%</td>
<td>.16</td>
</tr>
<tr>
<td>4-5</td>
<td>2.0%</td>
<td></td>
</tr>
</tbody>
</table>

*von Hertzen et al. Lancet 2002;360:1803*
Yuzpe Regimen: PREVEN™

**PREVEN Emergency Contraceptive Kit**

**Step 1**
- Read the instructions in the Patient Information Booklet carefully.

**Step 2**
- Use a pregnancy test.

**Step 3**
- Take emergency contraceptive pills as directed.

- **First Dose:** Take 2 pills during the first 72 hours after intercourse.
- **Second Dose:** Take remaining 2 pills 12 hours after the first dose.

Each tablet contains Levonorgestrel 0.25mg/Ethinyl Estradiol 0.05mg.

**Yuzpe Regimen: OC Formulations**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Pills/Dose</th>
<th>Levo Dose</th>
<th>Ethinyl Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coral</td>
<td>2 white</td>
<td>100</td>
<td>0.06</td>
</tr>
<tr>
<td>Alesse</td>
<td>5 pink</td>
<td>100</td>
<td>0.06</td>
</tr>
<tr>
<td>Levlen</td>
<td>5 pink</td>
<td>100</td>
<td>0.06</td>
</tr>
<tr>
<td>Nordette</td>
<td>4 light orange</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Levlen</td>
<td>4 light orange</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Levora</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Levoral</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Nordette</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Levora</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Nordette</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Levora</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Nordette</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
<tr>
<td>Levora</td>
<td>4 white</td>
<td>120</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**Yuzpe Regimen: Efficacy**

- **1999 – Trussell J, et al., meta-analysis of 8 studies, including a large international WHO trial.**
- Yuzpe results in an approximate 75% reduction (range 63%-79%) in the number of pregnancies estimated to occur without treatment.


**Yuzpe Regimen: Side Effects**

- Side effects:
  - Nausea (50%)
  - Vomiting (20%)
  - Heavy menses/Breast tenderness
- Use of antiemetic 1 hour before first dose decreases nausea and vomiting.
- Menses occurs within 3 weeks of therapy in up to 98% of women.
- No evidence of teratogenicity (based on combined OC data).


**Yuzpe Regimen: Contraindications**

- FDA, WHO, ACOG – Known pregnancy
- FDA – Relative (based on OC labeling, but no data available)
  - Clotting problems, venous thromboembolism, ischemic heart disease, stroke, migraine, liver tumors, breast cancer, breast biopsies


**Plan B: Progestin-Only Emergency Contraception**

- **First Dose:** Take one tablet within 72 hours of unprotected intercourse.
- **Second Dose:** Take remaining tablet 12 hours after first dose.

Plan B: Progestin-Only EC

- Levonorgestrel 0.75 mg taken twice, 12 hours apart (traditional, two-dose administration)
- Unlabeled equivalent
  - 20 pills/dose of Ovrette taken 12 hours apart
- More effective/fewer side effects than Yuzpe
- Data indicate a single dose of 1.5 mg levonorgestrel is as effective and causes similar side effects as traditional two-dose levonorgestrel
- Mechanism of action is inhibition of ovulation


Proportion of Pregnancies Prevented by Levonorgestrel vs. Yuzpe Regimen*

Levonorgestrel: 74% vs. Yuzpe: 71%

Levonorgestrel and Yuzpe Regimens: Delay of Treatment and Pregnancy Rates

Levonorgestrel vs. Yuzpe: Side Effects

- Nausea: Levonorgestrel 51%, Yuzpe 23% (Significant at p<0.01)
- Vomiting: Levonorgestrel 10%, Yuzpe 6%
- Dizziness: Levonorgestrel 17%, Yuzpe 11%
- Fatigue: Levonorgestrel 17%, Yuzpe 29%

Levonorgestrel vs. Mifepristone: Efficacy*

Levonorgestrel: 82% vs. Mifepristone: 77% vs. Levonorgestrel: 81%

*Prevented fraction of pregnancies estimated to occur without treatment

Copper IUD for EC

- Second-line method
- Estimated failure rate ≤0.1% (based on 8,400 postcoital insertions)
- Mechanism(s) of action
  - Impairs fertilization
  - Alters sperm motility and integrity
  - Impairs implantation

Mifepristone (RU 486)

- Synthetic steroid that prevents progesterone from binding to progesterone and glucocorticoid receptors
- Mechanism(s) of action
  - Disrupts follicular maturation and endocrine function of the granulosa cell
  - Disrupts midcycle LH surge
  - Interrupts hormonal support of the endometrium, making it asynchronous

Mifepristone: Efficacy

- Glasier, et al, 1992
  - 800 women and adolescents
  - Single 600 mg dose given within 72 hours of unprotected coitus was 100% effective
- WHO 1999
  - 1,700 women
  - 10 mg and 50 mg mifepristone equal in efficacy to 600 mg dose (85% decrease in number of pregnancies estimated to occur without treatment)
  - Effective up to 5 days after unprotected sex

Mifepristone: Side Effects

- Less nausea and vomiting than Yuzpe
  - Nausea: 40% vs. 60%
  - Vomiting: 3% vs. 17%
- More delay of menses than Yuzpe
  - Delay menses >7 days: 42% vs. 13%
- Nausea & vomiting similar to levonorgestrel
- More delay menses >7 days: 9% vs. 0% [mifepristone vs. two-dose levonorgestrel]
Mifepristone vs. Yuzpe*: Side Effects

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Mifepristone</th>
<th>Yuzpe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea Day of Treatment</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Nausea After Day of Treatment</td>
<td>28%</td>
<td>17%</td>
</tr>
<tr>
<td>Vomiting Day of Treatment</td>
<td>46%†</td>
<td>27%‡</td>
</tr>
<tr>
<td>Headache at Any Time</td>
<td>60%†</td>
<td>53%‡</td>
</tr>
<tr>
<td>Breast Tenderness at Any Time</td>
<td>40%</td>
<td>70%‡</td>
</tr>
</tbody>
</table>

*Ethinyl estradiol + norgestrel † Significant at p<0.001 ‡ Significant at p<0.002


Delay of Menses* by Dose of Mifepristone for Emergency Contraception

- 600 mg: 46%† Delay >7 days
- 50 mg: 23%
- 10 mg: 18%


Mifepristone vs. Yuzpe: Side Effects

Mifepristone Prescribing for EC

- FDA approved as abortifacient October 2000
- Can legally be prescribed off label as EC
- Only available in the 200 mg dose (50 mg and 10 mg just as effective as 600 mg for EC with fewer side effects)
- Limited prescriber availability (FDA prescriber agreement required)

FDA Prescriber’s Agreement Available at: http://www.fda.gov/cder/drug Infopage/mifepristone/

Emergency Contraception: Rx by Telephone

- 3 questions to ask:
  - Have you had unprotected sex or a problem with your birth control (such as condom breakage) during the last 3 days (rule out sexual assault)?
  - Did your last menstrual period begin less than 4 weeks ago?
  - Was the timing and duration of your last menstrual period normal?
- If the patient responds “yes” to all 3 questions, a clinician may prescribe emergency contraception over the telephone

Adapted from ACOG, Emergency Contraception: A Resource Manual for Providers, 1998

Emergency Contraception: Barriers

- Rx or Pharmacist dispensing creates delay
  - Woman must:
    - Identify the need for EC
    - Locate a prescriber
    - Call/visit prescriber
    - Find a pharmacy that stocks the product (discuss EC with pharmacist in pharmacy-access states)


Patient Counseling for EC

- How to take medication (give written instructions when possible)
- Use of antiemetic (Rx or OTC) 1 hour prior to first dose of Yuzpe
- Expected side effects (nausea/vomiting/cramping)
- When to expect menses (up to 98% bleed within 21 days of EC)
- If no menses after 3 weeks, rule out pregnancy
- May discuss contraceptive needs, STD protection, follow-up if EC fails


FDA transcripts. Available at: http://www.fda.gov/ohrms/dockets/ac/03/transcripts/4015T1.DOC
**Plan B™: Rx Data**

- 20,000 Rxs/month for Plan B
- 5 Pharmacy-access states
  - Washington, California, Alaska, New Mexico, Hawaii
- Washington: only 26% of pharmacies and 23% of pharmacists participate in the access program
- California: only 14% of pharmacies participate
- Albuquerque, NM: 89% of pharmacies did not carry Plan B; only 47% could access within 24 h
- Pennsylvania: only 35% of pharmacies could get Plan B or PREVEN within 24 h

**Advance Provision of EC**

- Glasier and Baird 1998
  - 553 given advance supply of EC pills
    - 187 (47%) used at least once; 98% correctly
    - 18 unintended pregnancies
    - 522 told to obtain EC pills when needed by visiting a physician
      - 87 (27%) used at least once
      - 25 unintended pregnancies
    - Neither group experienced adverse events
    - No difference in use of other contraceptives

**Advance Provision of EC: Teens**

- 301 minority, low-income women age 15-20 years
- Advance provision vs. instructions on how to get EC
  - At 1 month, the advance Rx group reported nearly twice as much EC use as control group (15% vs. 8%, p=0.05)
  - Advance EC group began EC significantly sooner (11.4 h vs. 21.8 h, p=0.005)
- No detrimental effects on condom or hormonal contraceptive use/no increase in unprotected intercourse

**FDA Rejects Plan B OTC**

- Reproductive Drugs and OTC Advisory Committees met Dec 16, 2003
  - Voted “Yes” to place Plan B OTC (23 to 4)
  - Plan B is safe, effective, and easy to use
  - FDA sent manufacturer a Non-Approvable Letter in May 2004
- ACOG and other organizations express dismay at the FDA’s decision, suggesting political agenda

**The Setting**

- 3.0 million unintended pregnancies each year in the United States: half (48%) of all pregnancies
- Half (48%) of women aged 15-44 have ever had an unintended pregnancy
- Emergency contraception has the potential to reduce unintended pregnancy significantly
- Emergency contraception is highly cost-effective

**Potential Impact**

- Reduce unintended pregnancies by half 1.5 million fewer
- Reduce abortions needed by half 0.7 million fewer
- Reduce pregnancies after rape by 88% 22 thousand fewer
Actual Impact

- In 2000, 1.3% of women having abortions reported using ECPs to prevent that pregnancy.
- 35% of those using ECPs had used no method of contraception in the month they became pregnant; 65% used ECPs for backup contraception.
- Up to 51,000 abortions were averted by use of ECPs in 2000

The Problem: Why a 25-Year Delay?

- Companies did not market pills or IUDs for emergency contraception in the U.S.
- Clinicians do not routinely counsel women (or men) about emergency contraception
- Women (and men) do not know about emergency contraception

The Solution

- Market EC
  - marketing promotes awareness
  - specifically packaged products are less confusing for users and providers, and may reduce chances of incorrect prescribing or use
- Change provider practices
  - counsel women and men in advance
  - provide ECPs in advance
- Educate women and men
- Change from Rx to over/behind the counter

The Value of a Dedicated Product

- Ovral
- Preven
- Alesse

Emergency Contraception in Europe

- PC4 Schering
- Postinor-2 Gedeon Richter

Plan B

Ovrette
Emergency ContraceptionBTC

- ECPs are available directly from pharmacists without having first to get a prescription from a clinician in:
  - California
  - Washington State
  - Alaska
  - Maine
  - New Mexico
  - Hawaii
  - Parts of Canada
  - Belgium
  - Denmark
  - France
  - Portugal
  - South Africa
  - Sweden
  - United Kingdom

Pharmacists Providing ECPs

Response to Enhanced Availability: Washington State

- 10,000 patient visits per year
- 42% of visits were during evenings, weekends, or holidays
- 95% of women had sufficient opportunity to ask questions
- 85% of women were satisfied with the ongoing contraceptive counseling provided by pharmacists
- Medicaid projects annual savings of up to $10 million

California Pharmacy Access Partnership

- Effective January 1, 2002
- Pharmacists can provide EC without a prescription
- Collaborative agreements with local physicians
- Minors can receive EC services in pharmacies
- 500+ pharmacies statewide by 12/31/2002
- Based on Washington State Model (1998)

Planned Parenthood State Hotlines

Prescriptions are called in to the client’s pharmacy of choice
- Connecticut: 1-800-230-PLAN
- Georgia: 1-877-ECPIlls
- Illinois: 1-866-222-EC4U
- Maryland: 1-877-99-GO-4-EC
- North Carolina: 1-866-942-7762
Planned Parenthood State Hotlines

Prescriptions are called in to the client’s pharmacy of choice
- Georgia: www.ecconnection.org
- Illinois: www.plannedparenthoodchicago.com
- Indiana: www.ppin.org/ecaccess.com/ecinfo.html
- Oregon: www.ppcw.org

Providing EC is Now the Medico-Legal Standard of Care

- ACOG Practice Pattern on ECPs (12/96) established the professional standard of care
- FDA notice in Federal Register on ECPs (2/97) declared 6 (now 13) brands of regular OCs to be safe and effective for use for emergency contraception
- FDA explicitly approved Preven and Plan B as dedicated products, but FDA still recognizes 13 brands of regular combined OCs to be safe and effective for use for emergency contraception

Provider Practice: Good News

- Ever prescribed ECPs: OB/GYNs 80%, FPPs 60%
- Prescribed ECPs Last Year: OB/GYNs 80%, FPPs 60%

Provider Practice: Bad News

- Prescribed More Than Five Times Among Those Who Prescribed: OB/GYNs 20%, FPPs 10%
- Routinely Discuss EC: OB/GYNs 80%, FPPs 20%

The Clinical Bottleneck

- Clinicians overwhelmingly think ECPs are safe and effective, and the majority have prescribed in the last year
- Clinicians are waiting for women to ask for EC

The Clinical Bottleneck (cont)

- But women do not know to ask
  - while 76% of women have heard of ECPs/morning-after pills
  - only 16% of women know 72-hour time frame
  - only 2% of women have ever used ECPs
Educate Women

- Emergency Contraception Hotline
  – 1-888-NOT-2-LATE

- Emergency Contraception Website
  – http://not-2-late.com

- Public education media campaigns

---

Providers on the Hotline and Website

---

Public Education Campaign Messages

- There is something that can be done after unprotected sex to prevent pregnancy
- To find out more call: 1-888-NOT-2-LATE
- There is a 72-hour time limit
Resources: Emergency Contraception

- Hotlines
  - 1-888-NOT-2-Late or 800-584-9911
- Web Sites
  - http://www.NOT-2-Late.org
  - http://www.PREVEN.com
  - http://kaisernetwork.org
  - http://ecinfo/html/updates.htm (emergency contraception newsletters)
  - http://www.acog.org

Summary

- Unintended pregnancy/induced abortion are major problems in the United States
- Reliable and easy-to-use emergency contraceptive methods are available (Plan B, PREVEN)
- The Alan Guttmacher Institute estimates that in 2000 EC prevented 50,000 induced abortions
- Single dose levonorgestrel first-line method, followed by two-dose levonorgestrel, then Yuzpe
- In May 2004, the FDA rejected its scientific advisory panel’s recommendation to switch Plan B to OTC
- ACOG’s public education campaign, “Every Woman, Every Visit” will continue to urge Ob/Gyns to provide advance prescriptions for EC at every office visit

Medical Advisory Committee

- Don Downing, RPh
  Univ of Washington School of Pharmacy
  Renton, WA
- David A. Grimes, MD
  Family Health International
  Durham, NC
- Edith Guilmot, MD
  Family Planning Clinic and Public Health
  Ste Foy, Quebec
- Elizabeth Raymond, MD, MPH
  Family Health International
  Durham, NC
- Sharon Schnare, FNP, CNM
  Olalla, WA
- Felicia Stewart, MD
  Center for Reproductive Health Research & Policy, UCSF
  San Francisco, CA
- James Trussell, BPhil, PhD
  Princeton University
  Princeton, NJ

Sponsored by Association of Reproductive Health Professionals

This presentation is made possible by an unrestricted educational grant from the Open Society Institute